Medical Progress

Perspective on Hypertension in the Elderly

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More than half of elderly men and women have hypertension, leading to a significant risk of increased morbidity and mortality. The cause of hypertension in this age group is unknown. Left ventricular hypertrophy is frequently present, often associated with diastolic dysfunction. Systolic hypertension in the elderly increases the risk of cardiovascular disease, but there are no good data to show that the treatment of isolated systolic hypertension reduces the morbidity or mortality. Good evidence indicates that antihypertensive treatment in this group decreases cardiovascular morbidity and mortality up to age 80, so most elderly hypertensive patients should be treated. An empiric trial of nonpharmacologic therapy can be initiated in those with mild hypertension and no cardiovascular disease, but most patients will require drug therapy. Most elderly hypertensive patients have accompanying illnesses for which they may or may not be taking medications. Some antihypertensive drugs exacerbate coexisting diseases while others augment treatment regimens. Similarly, drugs may interact in a beneficial or adverse way. Finally, drug metabolism is altered by age, leading to problems with toxicity or diminished efficacy. The choice of medication should be based on all such considerations, including the cost and convenience of the drugs available.

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Physicians' goals are to prevent disease when possible, to treat disease when present, and to help each patient maintain the highest quality of life possible. These hold true for all patient populations but seem to have special significance in the geriatric population where physicians strive to maintain function and independence and to prevent disability or premature mortality. In the elderly, hypertension is the single most potent, common, and remedial risk factor for cerebrovascular disease, congestive heart failure, and coronary artery disease—the major causes of cardiovascular morbidity and mortality in those older than 65.[1] Hypertension and its sequelae become more important as our geriatric population increases in number.

Although the elderly currently represent only 15% of the United States population, they consume a third of the health care dollar. The elderly population is growing two and a half times faster than the general population. The geriatric population (those older than 65) has been estimated to approach 30 million by this year.[2] Although we anticipate an evolution in the delivery and funding of health care in the years to come, the problem presents itself now: that of treating a common disorder, hypertension, in a rapidly growing population, the elderly.

Hypertension and the Elderly

Just how common is hypertension in the elderly? The prevalence depends on the blood pressure criteria selected to define hypertension and the number of blood pressure measurements required to make the diagnosis. The risk from increasing levels of blood pressure parallels the rise in the systolic and diastolic blood pressures. The gradient of risk for each increment in blood pressure is greater with advanced age.[3] To estimate the rates or prevalence of hypertension, categories of normal, borderline, and high must be selected. Table 1 shows a simple classification scheme to categorize hypertension.[4] Because criteria to define hypertension vary, the reported prevalence of hypertension in the elderly depends on the definition. In the late 1970s, the National Health and Nutrition Survey evaluated an ambulatory population aged 65 to 74 years. The investigators chose to measure the blood pressure three times in a single visit and defined hypertension as an average pressure of greater than 140/90 mm of mercury. The overall prevalence of hypertension was 64.3%. When hypertension was defined as an average pressure of greater than 165/95 mm of mercury, the overall prevalence fell to 45.1%. As a rule, black women tended to have the highest prevalence of hypertension and white men had the lowest.[5] The 1988 report of the Joint National Committee estimated that by this year (1990), 45% of patients older than 65 would have a systolic blood pressure of greater than 160 mm of mercury or a diastolic blood pressure of more than 95 mm of mercury. If hypertension is defined as greater than 140/90 mm of mercury, the prevalence increases to 67%. In general, these figures are in agreement with several recently published articles that suggest that the prevalence of hypertension in the elderly ranges from 40% to 65%.[2,6-9]

Most clinical studies cite a 6% to 10% prevalence of isolated systolic hypertension (systolic blood pressure >160 mm of mercury with diastolic blood pressure <90 mm of mercury).[2] Kuramoto's study of 1,561 consecutive autopsies of patients aged 60 to older than 90 years revealed that 18% had isolated systolic hypertension and 37% had combined systolic and diastolic hypertension. While the percentage of patients with diastolic hypertension remained stable from

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TABLE 1.—*Classification of Hypertension in the Elderly Based on the Level of Systolic and Diastolic Blood Pressures*

Classification	Blood Pressure (BP), mm of mercury	
	Systolic	Diastolic
Combined hypertension	>160	>90
Borderline hypertension	140-159	>90
Predominantly systolic hypertension	>(diastolic BP−15)2	>90
Isolated systolic hypertension	>160	<90

age 60 on, the percentage of those with isolated systolic hypertension rose steadily from 7% to greater than 30% between the ages of 60 and 90.[9] Although the prevalence of isolated systolic hypertension is not as high as the prevalence of combined systolic and diastolic hypertension, it poses a major problem for elderly patients. The Framingham data indicate that the systolic blood pressure correlates better with the occurrence of ischemic heart disease, congestive heart failure, and atherothrombotic brain infarct than the diastolic blood pressure or mean arterial pressure.[10] In the European Working Party on High Blood Pressure in the Elderly trial, only the systolic blood pressure was associated with increased cardiovascular events in elderly hypertensive subjects.[11] High systolic pressures increase cardiac work, with the subsequent development of left ventricular hypertrophy and congestive heart failure. Clinicians should evaluate the baseline systolic blood pressure and attempt to reduce the systolic and the diastolic pressures in elderly persons with combined diastolic and systolic hypertension. Treatment aimed at lowering the systolic blood pressure should improve cardiac function and decrease the development of heart disease with its associated morbidity and mortality. Clinical studies to prove the efficacy of the treatment of isolated systolic hypertension are underway.

Although a rise in blood pressure with increasing age is not inevitable, persons living in industrialized nations such as the United States exhibit a rise in both diastolic and systolic blood pressures with advancing age.[12,13] Socioeconomic, cultural, and behavioral factors such as smoking, ethanol use, obesity, exercise patterns, diet, and stress may account for the time- and age-related rise in blood pressure. In the United States the systolic blood pressure rises 5 to 10 mm of mercury from ages 40 through 80. The diastolic blood pressure rises 5 to 6 mm of mercury to age 50 through 60, then levels off as a person ages.[14] Women and blacks have the sharpest rise in both systolic and diastolic blood pressures compared with whites and men, whose pressures rise the slowest. Those who have a low or normal blood pressure as young adults show the least tendency to have hypertension with age.[15]

Risk of Hypertension in the Elderly

As stated before, cerebrovascular disease, congestive heart failure, and coronary artery disease are the major causes of morbidity and mortality in the elderly. In fact, greater than 50% of all mortality beyond age 65 is a result of cardiac or cerebrovascular disease. An estimated 40% of patients aged 65 through 74 have cardiac disease; the number rises to 50% for those older than 75. As the blood pressure increases, so does the risk of a cardiovascular event.[16] Not only are elderly persons more likely to have cardiovascular disease develop, but they are also more likely to succumb to an event. Advanced age significantly affects the survival after a stroke or myocardial infarction. A 60- to 69-year-old patient with a myocardial infarction has a 38% mortality rate, but a patient aged 80 to 89 has a 58% mortality.[17] Only 20% of patients older than 60 with stroke have a good outcome in contrast to younger stroke patients who show a favorable outcome in 30% to 50% of cases.[18] Cardiovascular mortality increases eight times in hypertensive women and two times in hypertensive men aged 65 to 74 compared with normotensive controls of the same age.[19] Several studies have shown that both combined systolic and diastolic hypertension and isolated systolic hypertension are significant risk factors for cardiovascular morbidity and mortality in the elderly.[20]

Etiology of Hypertension in the Elderly

No one knows what causes hypertension in the elderly. The aging process itself is not entirely responsible for the development of hypertension. Remember, not all elderly persons have hypertension, but the aging process does have an effect on all major organ systems including the heart, aorta, peripheral vasculature, kidneys, and central nervous system. Changes in the body composition and chemistry with alterations in microanatomy and dynamic mechanical properties of various organ systems contribute to the complex process of aging. Some of these changes are theorized to play a part in the development of hypertension in the elderly. Hypertension in a geriatric patient is characterized by a low cardiac output and high peripheral vascular resistance.[21] The aortic wall thickness increases with age, and elasticity decreases. The aorta becomes elongated and tortuous with an increase in diameter and volume. The increase in aortic cross-sectional area results in an increase in vascular stiffness.[22] The left ventricle must pump against a stiff aorta and high peripheral vascular resistance. As a result the left ventricular end-diastolic volume increases, the stroke volume falls, and the cardiac output falls.[23] Elderly patients with hypertension are also noted to have lower intravascular volume, renal blood flow, and plasma renin levels than young hypertensive persons.[21] With increased age comes a decrease in the glomerular filtration rate and impaired sodium-conserving ability, diluting capacity, and baroreceptor sensitivity.[24,25] The baroreceptor reflexes are responsible for attenuating sudden increases or decreases in the arterial blood pressure with changes in posture.[26] Faulty autoregulation in blood pressure through alterations in baroreceptor reflex mechanisms may play some part in the development of hypertension in the elderly. It may also explain, in part, the tendency of older patients to have labile hypertension or orthostatic hypotension. The decrease in lean body weight with an increase in total body fat seen in most older patients may contribute to the development of hypertension.[27] A sedentary life-style with decreased physical activity may also play a part. It is difficult to know which of these observations are related purely to normal aging and which are related to hypertension. There have been no good age-matched studies to compare elderly normotensive and hypertensive subjects. Hypertension in the elderly remains a common disorder, extensively studied and poorly understood.

Diagnosis of Hypertension in the Elderly

Most clinicians agree that a diagnosis of hypertension can be made only after three blood pressure measurements taken on three separate visits show pressures at or above a level

previously determined to define hypertension—usually above 140/90 mm of mercury.[28] There is some question about the accuracy of indirect (cuff) blood pressure measurements in the elderly. The young show no important difference in blood pressure whether it is measured directly (intra-arterial pressure) or indirectly. In the elderly, indirect blood pressure measurements underestimate the direct systolic blood pressure by 4 mm of mercury and overestimate the direct diastolic blood pressure by approximately 9 mm of mercury.[29] There is a consistent correlation between direct and indirect blood pressure measurements in each person. Most physicians never consider or measure the direct blood pressure. Instead, they use indirect measurements to diagnose hypertension and monitor therapy. The discrepancy between the direct and indirect blood pressure should be kept in mind when caring for elderly patients with hypertension. The blood pressure should also be measured standing and sitting to identify significant orthostatic changes.

Errors in Diagnosis

There are three major causes of misdiagnosing hypertension in the elderly: pseudohypertension, the auscultatory gap, and "office" or "white coat" (labile) hypertension.

One investigator suggests that as many as 15% of patients older than 65 may have pseudohypertension.[30] In the elderly sclerotic, rigid arteries may develop that compress only at high pressures. If the vessels of the arm are sclerotic, artificially high blood pressures will be obtained with a sphygmomanometer (pseudohypertension). The difference between cuff and intra-arterial blood pressures may vary from 10 to 100 mm of mercury. The Osler maneuver allows the detection of pseudohypertension.[31] To do the Osler maneuver, the clinician palpates the radial artery while inflating the blood pressure cuff. When arterial pulsations stop, the artery is assessed. If it remains rigid and palpable, the diagnosis of pseudohypertension is made. Treating patients who have pseudohypertension may be dangerous without an accurate determination of the blood pressure measured intra-arterially.

In the elderly there is often a wide gap between the first Korotkoff's sound and subsequent auscultated beats (the auscultatory gap). If the blood pressure cuff is inflated into this quiet gap, or if the first sound is not recorded, the systolic blood pressure will be underestimated. Accurate systolic pressures can be obtained by inflating the cuff to the point the palpable pulse disappears, then reinflating the cuff to this value and listening for the first Korotkoff's sound, which represents the true systolic blood pressure.

White coat or office hypertension is a transient increase in blood pressure associated with a visit to a physician's office. Patients with office hypertension usually have normal blood pressures outside the office with peaks in pressure at times of stress.

Clinical Evaluation

A complete evaluation of an elderly patient with hypertension includes not only the blood pressure measurement but a careful history and physical examination. The patient should have the blood pressure measured in the sitting and standing positions, and an Osler's maneuver should be done. Evidence of cardiac enlargement or failure and signs or symptoms of renal failure should be sought. The history should include questions concerning smoking habits, diet and exercise habits, alcohol intake, and drug history. Although there are no screening or standard laboratory tests, many clinicians find a complete blood count, a chemistry profile with serum creatinine and cholesterol levels, a urinalysis, and an electrocardiogram useful.[16] Secondary causes of hypertension are not common in the elderly, but when a patient presents with hypertension after the age of 55, a blood pressure that is difficult to control despite appropriate three-drug therapy, resistance to an antihypertensive regimen previously effective, or accelerated hypertension, secondary sources should be considered. If the serum creatinine level rises substantially in a patient receiving an angiotensin-converting enzyme inhibitor, bilateral renal artery stenosis should be considered and an appropriate workup done. An echocardiogram or gated blood pool scan may be indicated to help guide therapy in patients with congestive heart failure, especially if the patient is to be treated with antihypertensive agents that have adverse inotropic or chronotropic effects.

Decision to Treat

The decision to treat a patient who has hypertension involves assessing the risk-benefit ratio. In most hypertensive elderly patients, the benefits of treating hypertension outweigh the risks and side effects. Several well-done clinical trials show that antihypertensive therapy is effective in lowering the blood pressure in the elderly and that cardiovascular morbidity and mortality are reduced in patients who achieve goal blood pressures.

Clinical Trials

The Hypertension Detection and Follow-up Study, a community-based, randomized, controlled study, compared referred-care (private practice) to stepped-care (special care) treatment in patients with elevated diastolic blood pressures.[32] A total of 2,376 patients aged 60 through 69 were involved. The study showed that patients receiving stepped care—a combination regimen of spironolactone or chlorthalidone with reserpine or methyldopa, followed by hydralazine hydrochloride, then guanethidine monosulfate as needed to control the blood pressure—reached or surpassed their blood pressure goal (diastolic blood pressure <90 mm of mercury) in 60% to 75% of cases. The referred-care group—treated with an unstructured regimen by private physicians—reached their goal pressure in only 34% to 55% of cases. As a rule, the elderly patients were more likely than younger patients to reach their goal pressures. All patients showed some benefit from treatment. The stepped-care group had a lower mortality than the referred-care group and were more likely than referred-care patients to remain on active treatment for five years (79.4% compared with 54%, respectively). For those aged 60 to 69, total mortality was 16.4% lower in the stepped-care group than in the referred-care group. This was close to the 16.9% reduction in mortality for all groups. There was a 45% reduction in the incidence of fatal and nonfatal strokes but no differences in that of fatal coronary artery disease or nonfatal myocardial infarction.

The Veterans Administration Cooperative Study and the Australian Therapeutic Trial in Mild Hypertension were both studies using stepped care.[33,34] The Australian study was a single-blind, placebo-controlled, parallel trial that included 582 healthy patients aged 60 through 69 with diastolic blood pressures of 95 to 100 mm of mercury and systolic blood

pressures of more than 200 mm of mercury. The investigators first administered chlorothiazide followed by methyldopa, pindolol, or propranolol hydrochloride as needed. If the diastolic blood pressure was still elevated, clonidine hydrochloride or hydralazine hydrochloride was added. The patients on drug therapy had a mean fall in diastolic blood pressures of 13 mm of mercury compared with the patients receiving a placebo who showed a 7-mm-of-mercury drop in diastolic pressures. The trial end points were death or a specific cardiovascular event. Overall there was a 39% decrease in the number of trial end points in the elderly treated group. The improved outcome was mostly attributable to fewer cerebrovascular and nonfatal cardiovascular events.

The Veterans Administration trial was a double-blind, placebo-controlled trial in which pharmacologic treatment (hydrochlorothiazide, reserpine, and hydralazine) and nonpharmacologic treatment (salt restriction) were used to control blood pressures. The original study included 194 control patients and 186 treated patients (only men in both groups). Treated patients and control patients had initial diastolic blood pressures averaging 90 to 114 mm of mercury. Of all patients enrolled, 81 were older than 60 years. In this group of elderly patients, 62.9% of patients in the control group had morbid cardiovascular events develop compared with 28.5% in the treated group. Those with the highest blood pressure and a history of cardiovascular disease benefited the most. In each of these studies, subgroups of elderly patients were evaluated to determine the efficacy of treatment.

None of these studies, however, was designed specifically to evaluate the effect of treating hypertension in elderly patients. In contrast, the European Working Party on High Blood Pressure in the Elderly trial, as the name suggests, was designed to do that.[35] A total of 840 hypertensive men and women (blood pressures 160 to 239/90 to 119 mm of mercury) older than 60 were enrolled. A third of the patients had cardiovascular complications on entry. In a double-blind, random manner, patients received a placebo or drug (hydrochlorothiazide and triamterene). The dosage of the "diuretic" pill (placebo or drug) could be increased to two capsules per day, and methyldopa (placebo or drug) could be added to control the blood pressure as deemed necessary. After five years of treatment, blood pressures in the actively treated group fell from $183 \pm 17/101 \pm 7$ to $105 \pm 20/85 \pm 9$ mm of mercury (mean $\pm$ standard error of the mean). In the placebo group, pressures fell less impressively from $182 \pm 16/101 \pm 7$ mm of mercury to $171 \pm 25/95 \pm 9$ mm of mercury. Overall, active drug treatment reduced the cardiac mortality by 38% and cardiovascular mortality by 27%. The number of other nonfatal cardiovascular events was decreased 60% in patients receiving active treatment, mostly because of a 63% decrease in the incidence of severe congestive heart failure. There was a 52% reduction in the number of cerebrovascular events (but not mortality) in actively treated patients. These patients also showed a 90% decrease in the number having severe hypertension develop. Although there was no decrease in the number of myocardial infarctions, there were fewer fatal infarctions and a decrease in the incidence of sudden death in patients on drug treatment. A beneficial effect of active treatment was seen in men and women at all levels of systolic blood pressures, in smokers and nonsmokers, and in those with and without cardiovascular complications at the time of enrollment. There were data to suggest that even those with the mildest hypertension benefit from treatment, but the numbers were not statistically significant. In the actively treated group, there was a mild increase in fasting blood glucose and serum creatinine levels and a mild decrease in serum potassium levels. Patients receiving placebo showed a slight decrease in fasting blood glucose levels and a smaller rise in serum creatinine levels. All of the changes were clinically modest and only some were statistically significant.

After reviewing these studies, it seems reasonable to conclude that, for most patients aged 60 to 79 with mild or moderate hypertension (blood pressure >160/90 mm of mercury), the benefits of treating their hypertension outweigh the risks and side effects. In those 80 years or older, treatment decisions must be tailored to each person.[35] If the patient is a "young 80" or if disease or risk factors exist that can be exacerbated by hypertension, then treatment is usually indicated. Patients with borderline hypertension (140 to 160/90 to 95 mm of mercury) should be similarly evaluated and treated appropriately.

Treatment Recommendations

Nonpharmacologic Therapy

When the decision to treat has been made, the issue of appropriate therapy arises. In young patients with mild hypertension, nonpharmacologic intervention is sometime sufficient to lower the blood pressure into the normal range. Similar therapy has not been studied in elderly patients with mild hypertension, but it seems logical to try before prescribing drugs. An elderly patient can be asked to lose weight, exercise regularly, and restrict sodium and alcohol intake without much, if any, risk to his or her health.[36]

Weight loss has historically been the most effective nonpharmacologic intervention used in young patients. Older patients typically have a higher proportion of total body fat and a lower lean body mass than younger counterparts. If an elderly patient is more than 130% of his or her ideal weight, a trial of weight loss may help lower the blood pressure.

Exercise conditioning of the elderly is possible, and, unless there are reasons not to recommend exercise, such activity should be encouraged.

Although several small studies indicate that a fair number of elderly persons with hypertension respond to low-sodium diets, restricting dietary sodium may or may not lower the blood pressure.

Restricting alcohol intake is indicated in hypertensive patients who consume more than 4 oz of alcohol per day. Not only will their general health improve, they will, in most instances, show a drop in blood pressure.

Oral calcium supplementation has been shown to be of some benefit in lowering the blood pressure. If a patient is taking calcium supplements for other reasons—that is, to prevent osteopenia—or if there is a good antihypertensive response to a trial of calcium, then supplementation should be continued. Many women are already taking calcium supplements; prescribing calcium for normocalcemic or hypocalcemic men is a low-risk intervention.

Pharmacologic Therapy

If nonpharmacologic treatment fails or a patient is ineligible for such treatment because of the blood pressure level, drug therapy is called for. The first drug chosen to treat young and middle-aged persons with hypertension has traditionally been hydrochlorothiazide. In elderly patients it is

important to consider the choice carefully and whether the drug of choice will treat other coexisting conditions or possibly exacerbate them. Other medical conditions, drug metabolism, and renal and hepatic function will usually dictate the drug choice. An effort should be made to tailor the treatment to each patient. By choosing simple drug regimens that can treat as many conditions as possible with the fewest number of medications, clinicians can increase compliance, help reduce adverse side effects, and minimize patients' confusion. In elderly hypertensive patients it is important to start with low drug doses and increase the dose slowly. The goal of therapy should be a blood pressure of less than 160/90 mm of mercury. Again the pressure should be lowered slowly to avoid sudden drops in blood pressure that can result in cerebral, coronary, and renal hypoperfusion.[36]

Diuretics

Based on the results of the European Working Party on High Blood Pressure in the Elderly trial, and in the absence of factors to recommend other drugs, therapy should be initiated with small doses of thiazide diuretics. In fact, the 1988 report of the Joint National Committee suggests that the elderly do well when treated with diuretics.[6] If there are no contraindications, a potassium-sparing diuretic may be used in combination with the thiazide to help control the blood pressure and maintain normal potassium levels. If renal failure is present, furosemide is a better choice. Dietary sodium restriction is recommended with diuretic treatment to minimize potassium losses and to enhance the antihypertensive effect. The average response rate in the elderly with this regimen is 60% to 70% whereas the average drop in blood pressure is 25/10 mm of mercury. Diuretic therapy is relatively cheap, easy to take, associated with few side effects, and effective in lowering the cardiovascular morbidity and mortality in the elderly. Therapy should be monitored closely to avoid dehydration, hypokalemia, and orthostatic hypotension.

β-Blockers

β-Blockers, although not as effective as other antihypertensive agents in controlling the blood pressure in geriatric patients, can be used effectively.[6,37] β-Blocker monotherapy is associated with a 20% response rate in patients 60 years of age.[33,38] Low-dose diuretic therapy may enhance the efficacy of β-blockers and minimize the fluid retention often associated with their use. β-Blockers are a poor choice in patients with reversible obstructive airways disease, diabetes mellitus with evidence of neuropathy, congestive heart failure, atrioventricular conduction abnormalities, bradyarrhythmias, depression, and allergic rhinitis. Conversely, patients with tachyarrhythmias, senile tremor, migraine headache, and a previous myocardial infarction may benefit doubly from using β-blockers. The metabolism of both the water-soluble β-blockers (nadolol and atenolol) and fat-soluble β-blockers (metoprolol tartrate and propranolol) may be altered in the elderly, resulting in higher plasma concentrations for a given dose of drug. Low doses are, therefore, recommended, with slow advancement as necessary. Fatigue and exercise intolerance may limit the use of β-blockers in the elderly.

Central α_2-Agonists

Central α_2-agonists (clonidine, methyldopa, guanabenz acetate, and guanfacine) are effective antihypertensive drugs and well tolerated in the geriatric population when used alone or in combination with a diuretic.[39] Adverse side effects include constipation, dry mouth, and sedation. The sedating effect of these drugs can be used to an advantage in patients who have difficulty falling asleep. Clonidine when used at bedtime can enhance sleep induction, minimizing daytime somnolence. In fact, because of the decrease in the glomerular filtration rate often seen in the elderly, the sustained effects from a single bedtime dose of clonidine make once-a-day dosing possible for some. If the drug is used twice a day, the evening dose should be greater than the morning dose. A relatively new product, transdermal clonidine, offers easy, effective blood pressure control with fewer side effects.[40] The patch, applied once a week, is usually well tolerated. Some patients may have a local reaction and are forced to discontinue the drug. The other central α_2-agonists, methyldopa, guanabenz, and guanfacine, are equally effective but not used as commonly as clonidine.

α_1-Receptor Antagonists

The α_1-antagonists, prazosin hydrochloride and terazosin hydrochloride, are effective antihypertensive agents in the general population.[41] Their use in the elderly has yet to be studied extensively. As a rule, the α_1-antagonists are associated with few side effects. The major side effect noted is hypotension, which is most likely to develop in those patients who are volume depleted and taking diuretics or other antihypertensive drugs. First-dose hypotension is a common phenomenon in all age groups. To avoid the adverse effects of this drop in blood pressure, patients should be instructed to take the first dose at bedtime and to remain in bed until morning. Similar precautions should be used when increasing the dose or restarting the drug after periods of withdrawal (usually initiated by the patient). The use of α_1-antagonists may increase urine flow in elderly men with symptoms of obstructive uropathy owing to an effect on the sphincter tone.[42]

Combination α- and β-Blockers

Labetalol hydrochloride, an α- and β-adrenergic blocker, is also an effective antihypertensive agent in the elderly.[43] As with the α_1-antagonists, the initial dose of labetalol should be small and given at bedtime. Orthostatic hypotension is the major adverse effect of αβ-blockers; therefore, the drugs must be used cautiously. Other side effects include nightmares, gastrointestinal disturbances, fatigue, and malaise.

Direct Vasodilators

Some clinicians choose to treat their elderly hypertensive patients with peripheral vasodilators such as minoxidil and hydralazine. Their use has not been tested extensively in the elderly, but they are effective in lowering blood pressures in younger subjects. The tachycardia and fluid retention associated with using vasodilators may limit their use in the elderly. Diuretics and β-blockers can help offset these effects in patients treated with multiple drugs.

Angiotensin-Converting Enzyme Inhibitors

The angiotensin-converting enzyme (ACE) inhibitors captopril, enalapril maleate, and lisinopril act as vasodilators. They decrease the total peripheral resistance and blood pressure without causing reflex tachycardia. Clinical studies show efficacy in the elderly without significant metabolic

effects of central nervous system side effects.[44] Angiotensin-converting enzyme inhibitors are a good choice in patients with hypertension and congestive heart failure as they have the added benefit of working to decrease the afterload and symptoms of failure. Because these drugs can cause hyperkalemia, they should be used cautiously in patients with renal failure or who are taking nonsteroidal anti-inflammatory drugs. The use of ACE inhibitors should probably be avoided completely in patients taking potassium-sparing diuretics or potassium salts. The serum creatinine level should be monitored because ACE inhibitors can impair renal function.

Calcium Channel Blockers

Another class of drug that offers effective blood pressure control and relatively few side effects in the elderly is the calcium channel blocker.[45,46] Available calcium channel blockers include verapamil hydrochloride, diltiazem, nifedipine, isradapine, nicardipine hydrochloride, and nitrendipine. Nitrendipine, isradapine, verapamil sustained-release, and diltiazem sustained-release are long-acting drugs that can be taken once or twice a day. The initial dose, as with other antihypertensive medications, should be low. The calcium channel blockers may decrease the mean arterial pressure as much as 25%, a potential problem for patients with compromised cerebral, coronary artery, or renal blood flow. Verapamil and diltiazem have a depressant effect on the sinus node and atrioventricular conduction. In patients with tachyarrhythmias, this is an advantage. All calcium channel blockers are cardiac depressants, although the degree of myocardial depression varies from drug to drug. Of nifedipine, diltiazem, and verapamil, nifedipine is the weakest cardiac depressant and verapamil is the strongest. Other major side effects include headache, gastrointestinal upset, tachycardia, dizziness, edema (without fluid retention), and constipation (seen most often with the use of verapamil).

All of the drugs discussed in this article are more effective when combined with small doses of a diuretic. If the simplest regimen is sought and a patient responds to therapy with one drug, then diuretics can be omitted. The point to be made is that all drugs must be administered carefully in elderly patients who frequently have altered metabolism and different responses to drugs than young patients. Table 2 outlines the dosages, cost, adverse side effects, special considerations, and drug interactions of the commonly available antihypertensive drugs.

Cost of Drugs

The cost of treatment is an important consideration in antihypertensive therapy in the elderly.[47] The total cost includes not only the purchase price of drugs, but also office visits to monitor the effect of treatment or to evaluate side effects and laboratory tests, such as serum potassium, glucose, and lipid level. If a drug is prescribed at an optimal dose that is proved effective at the first follow-up visit and requires no laboratory testing, the overall cost to the patient may be reasonable even if the drug chosen is not the least expensive.

TABLE 2.—*Estimated Cost of a Year's Supply of Antihypertensive Drugs at University Hospital Pharmacy, University of Colorado Health Sciences Center (Wholesale Price), November 1988**

Drug					
Generic	*Trade Name (Manufacturer)†*	*Tablet Size, mg*	*Daily Dose/d*	*Annual Cost, $*	*Cost Per Pill, $‡*
Hydrochlorothiazide (HCTZ)	Esidrix (Ciba-Geigy)	*25*, 50	25 mg	4§	0.01
Chlorthalidone	Hygroton (USV Pharmaceutical)	*50*, 100	25 mg	7§	0.02
Furosemide	Lasix (Hoechst-Roussel)	*40*, 80	40 mg, 2×	7§	0.01
Spironolactone	Aldactone (Searle)	*25*, 50, 100	25 mg, 4×	28§	0.02
Triamterene	Dyrenium (Smith Kline & French)	*50*, 100	50 mg, 2×	137	0.19
Triamterene/HCTZ	Dyazide (Smith Kline & French)	*25/50* capsule	1 capsule	43§	0.15
	Maxzide (Lederle)	*50/75* tablet	½ tablet	27	0.12
Amiloride HCl	Midamor (Merck)	*5*, 10	5 mg	47	0.13
Reserpine	Serpasil (Ciba-Geigy)	*0.1*, 0.2	0.2 mg	7§	0.02
Methyldopa	Aldomet (Merck)	*500*	500 mg, 2×	79	0.11
Clonidine HCl	Catapres (Boehringer Ingelheim)	0.1, *0.2*	0.2 mg, 3×	22§	0.02
Propranolol HCl	Inderal (Ayerst)	40, *80*	80 mg, 2×	14§	0.02
Metoprolol tartrate	Lopressor (Ciba-Geigy)	50, *100*	50 mg, 2×	140	0.39
Atenolol	Tenormin (Stuart)	50, *100*	50 mg	112	0.62
Labetalol HCL	Normadyne (Schering)	*200*, 300	200 mg, 3×	262	0.24
Prazosin HCl	Minipress (Pfizer)	1, *2*, 5	2 mg, 3×	280	0.26
Hydralazine HCl	Apresoline HCl (Ciba-Geigy)	10, 25, *50*	100, 2×	14§	0.01
Minoxidil	Loniten (Upjohn)	2, *5*, 10	5 mg, 2×	158	0.22
Captopril	Capoten (Squibb)	*25*, 50, 150	25 mg, 3×	302	0.28
Enalapril maleate	Vasotec (Merck)	5, 10, *20*	10 mg, 2×	245	0.68
Lisinopril	Prinivil (Merck)	5, 10, *20*	20 mg	180	0.50
Nifedipine	Procardia (Pfizer)	*10*, 20	10 mg, 3×	280	0.26
Diltiazem HCl	Cardizem (Marion)	*30*, 60	30 mg, 3×	237	0.22
Verapamil HCl	Calan SR (Searle)	*240*	240 mg	190	0.53
	Calan	40, 80, *120*	120 mg, 2×	51§	0.07

HCl=hydrochloride, SR=sustained release

*Retail cost to patients may be estimated at 40% to more than 100% markup above wholesale price. The retail costs to patients at an independent pharmacy are comparable to or less than at the University Hospital Pharmacy.

†Many of these drugs are made by more than one manufacturer. The selection of one manufacturer's product over another should not be construed as an endorsement of that product by either the authors or the editors of THE WESTERN JOURNAL OF MEDICINE.

‡The price per pill is based on the italicized pill size.

§Generic cost.

If the costs are high, an elderly patient may stop taking the medication or may take inadequate doses in an attempt to continue treatment. Table 2 illustrates the cost per pill and the annual cost of antihypertensive therapy for some commonly prescribed drugs. These figures were obtained from the University Hospital Pharmacy in Denver. Note that the prices listed are wholesale prices; the retail cost to the patient is much higher (40% to 100% markup). The cost is estimated to be similar nationwide.[48]

The three least expensive drugs are thiazide diuretics, reserpine, and hydralazine. Diuretics are effective in 60% to 70% of elderly hypertensive patients when used alone. The cost increases substantially if potassium salts or potassium-sparing diuretics are used or if laboratory monitoring is fre-

TABLE 3.—*Side Effects and Drug Interactions of Antihypertensive Medications*

Drug Category	*Generic Drug*	*Usual Dosage Range, mg/d*	*Adverse Side Effects*	*Special Considerations*	*Drug Interactions*
Thiazide diuretics	Hydrochlorothiazide	12.5-200	Hypokalemia; glucose intolerance; elevated levels of uric acid, cholesterol, triglycerides; sexual dysfunction; weakness; dehydration	May be ineffective in renal failure; low potassium level can cause digoxin toxicity	Can increase lithium levels; NSAIDs can antagonize the antihypertensive effect; ACE inhibitors blunt hypokalemia
	Chlorthalidone	25-100			
Loop diuretics	Furosemide	40-160	Same as thiazides plus ototoxicity and tinnitus	Effective in renal failure	Can potentiate the ototoxicity of aminoglycosides
Potassium-sparing agents	Spironolactone	50-100	Hyperkalemia; spironolactone use causes gynecomastia and mastodynia; triamterene use is associated with renal calculi	Spironolactone use interferes with digoxin immunoassay	ACE inhibitors and NSAIDs can potentiate hyperkalemia and precipitate renal failure; ↑ lithium levels
	Amiloride	5-20			
	Triamterene	100-300			
β-Adrenergic blockers	Propranolol HCl	80-320	May mask signs of thyrotoxicosis and hypoglycemia; may cause bronchospasm; fatigue, insomnia, sexual dysfunction, CHF, ↑ triglycerides, ↓ high-density-lipoprotein levels	Do not use in patients with asthma, CHF, heart block (more than first-degree), sick sinus syndrome; caution in patients with diabetes mellitus or COPD; need to be tapered to discontinue	Cimetidine use may ↓ bioavailability; hydralazine use may cause ↑ drug level (inhibits hepatic metabolism); β-blockers and reserpine drop blood pressure dramatically
	Metoprolol tartrate	100-450			
	Atenolol	50-100			
Centrally active blockers	Clonidine HCl	0.2, 0.6	Drowsiness, sedation, dry mouth, fatigue, sexual dysfunction, skin rash with patch	Rebound hypertension can occur with rapid withdrawal	Tricyclic antidepressants can ↓ effects of clonidine
	Clonidine TTS	1 patch/wk			
Peripherally acting blockers	Methyldopa	500-2000		Methyldopa may cause liver damage and Coombs'-positive hemolytic anemia;interferes with urine measurement of catecholamines;orthostatic hypotension	
	Prazosin	2-20	1st-dose syncope, orthostatic hypotension, weakness, palpitations		
Vasodilators	Hydralazine HCl	40-300	Vasodilatation associated with tachycardia, fluid retention; hydralazine use causes positive antinuclear antibody test; minoxidil causes hypertrichosis	May precipitate angina in patients with coronary artery disease; lupuslike syndrome with hydralazine; minoxidil use may cause or aggravate pleural or pericardial effusion; fluid retention aggravates CHF	
	Minoxidil	10-40			
ACE inhibitors	Captropril	50-150	Rash, cough, angioneurotic edema, hyperkalemia, dysgeusia; captopril use causes neutropenia, agranulocytosis, proteinuria	May precipitate acute renal failure in patients with bilateral renal artery stenosis	NSAIDs plus aspirin use potentiate potassium-sparing effects
	Enalapril maleate	5-40			
	Lisinopril	10-80			
Calcium channel blockers	Nifedipine	30-90	Edema, headache; nifedipine causes peripheral edema, tachycardia; all but nifedipine associated with constipation	Use calcium channel blockers carefully in patients with CHF, contraindicated in 2nd-degree and 3rd-degree heart block; diltiazem and verapamil use may cause liver failure	Quinidine use plus these drugs causes hypotension, especially in patients with IHSS; may ↑ digoxin levels; cimetidine use can ↑ nifedipine levels; ↑ prothrombin time with any of the 3
	Diltiazem HCl	90-360			
	Verapamil HCl	120-480			
	Verapamil HCl sustained-release	240-480			

ACE=angiotensin-converting enzyme, CHF=congestive heart failure, COPD=chronic obstructive pulmonary disease, IHSS=idiopathic hypertrophic subaortic stenosis, HCl=hydrochloride, NSAIDs=nonsteroidal anti-inflammatory drugs, ↑=increased, ↓=decreased

quently done. Generic propranolol, verapamil, and clonidine are relatively inexpensive, but there are no good data on the efficacy of these generics, and dosing several times a day is required for most. The newer drugs, such as the ACE inhibitors and calcium channel blockers, will be more costly but may require less frequent laboratory monitoring or fewer visits than the older, standard drugs for side effects or altered quality of life. Once again, cost must be considered and the choice tailored to the individual patient based on clinical and economic considerations.

Compliance in the Elderly

Treating the elderly can be rewarding, as most elderly patients take an active interest in their treatment and are, for the most part, compliant with therapy. Compliance varies with the number of drugs used and frequency of dosing. The best compliance—95%—is achieved with a one-drug regimen. Two-drug regimens are associated with a reported 84% compliance, while three-drug regimens are associated with 74% compliance—still good.[49] Elderly patients achieve their goal blood pressure more frequently than young patients yet do not suffer any increase in adverse drug effects. In one study, subjects aged 60 to 69 years had a lower five-year incidence of adverse reactions requiring discontinuation of a drug than did younger subjects: 29.8% and 34.38%, respectively.[50] Table 3 outlines common side effects and drug interactions associated with the various antihypertensive medications.

Isolated Systolic Hypertension

As stated earlier, isolated systolic hypertension is a risk factor for cardiovascular morbidity and mortality in the elderly. As an established risk factor, this condition should be treated, although benefit has yet to be established in controlled clinical trials. There is no consensus among physicians about the level of blood pressure that should be treated or a maximum age that may preclude therapy.[51,52] As a general rule, patients with a mean arterial pressure—determined by

$$MAP = DBP + [(SBP - DBP)/3]$$

of greater than 110 mm of mercury can safely be treated with antihypertensive drugs. If the mean arterial pressure is less than 110 mm of mercury, treatment may be somewhat risky. The medications used to treat isolated systolic hypertension can be expected to lower the systolic blood pressure 3 to 4 mm of mercury for each 1-mm-of-mercury drop in diastolic blood pressure.[53] The level of diastolic pressure can limit the treatment of isolated systolic hypertension. Because the coronary arteries fill during diastole, care must be taken in treating isolated systolic hypertension in patients with coronary artery disease. Nonpharmacologic and pharmacologic intervention can be used successfully to treat the disorder. The same drugs used to control combined hypertension can be used for patients with isolated systolic hypertension.

Summary

Hypertension in the elderly is a common disorder and an established risk factor for cardiovascular disease. Cardiovascular morbidity and mortality can be reduced in this population by bringing the blood pressure back to the normal range. Although a number of drug regimens are effective, an attempt should be made to individually tailor the treatment based on clinical characteristics and coexisting conditions. Therapy should be kept simple to minimize confusion and designed to maximize functional capacity and quality of life. The best outcome is obtained by a careful selection of drugs, considering age-related changes in metabolism, side effects, and other untoward effects likely to be found in the elderly. Finally, drugs should be prescribed in low doses with gradual increments in dose as needed to control blood pressure.

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